MicroRNA Regulation of Human Embryonic Stem Cell Self-Renewal and Differentiation

Grant Award Details

MicroRNA Regulation of Human Embryonic Stem Cell Self-Renewal and Differentiation

Grant Type: SEED Grant

Grant Number: RS1-00161

Investigator:

Name:	Robert Blelloch
Institution:	University of California, San Francisco
Type:	PI

Human Stem Cell Use: Embryonic Stem Cell

Award Value: $605,886

Status: Closed

Progress Reports

Reporting Period: Year 2

View Report

Reporting Period: NCE

View Report

Grant Application Details

Application Title: MicroRNA Regulation of Human Embryonic Stem Cell Self-Renewal and Differentiation

Public Abstract:

A major hurdle for regenerative medicine is the safe transplantation of human embryonic stem (ES) cells or their derivatives into patients. While the unlimited growth potential of ES cells is a major asset for their potential in tissue replacement, it is also a major risk for tumorigenesis. Therefore, it is critical to determine what molecules are responsible for silencing the tumorigenic risk of embryonic stem cell derivatives as occurs during the process of normal development. Identification of such molecules should provide both markers for tumorigenic risk as well as potential targets for therapeutic intervention when tumors do develop from transplanted tissue. We now know that most, if not all adult cells can revert to an early stem cell phenotype. This has been proven by a technique called somatic cell nuclear transfer, where adult cell nuclei are transferred into oocytes and allowed to develop as early embryos. These embryos reactivate the embryonic stem cell program within the adult nuclei. Cells derived from these embryos, the embryonic stem cells, have regained the ability to proliferate indefinitely, a property termed self-renewal. Therefore, considering there is in the order of one hundred trillion cells in the adult human, it is amazing that some fraction of cells do not commonly reactivate the stem cell program by chance. This is because human have evolved an amazing and complex network of molecules whose main purpose is to permanently silence critical components of the embryonic stem cell program. Unfortunately, this network is poorly understood. The aim of our laboratory and of this research proposal is to identify these factors and use them to our advantage. We have discovered in the mouse model that small RNA molecules called microRNAs are essential for the silencing of the embryonic stem cell's capacity to self-renew. In this grant, we propose to confirm a similar role for microRNAs in human ES cell differentiation. Furthermore, we propose to identify the molecular nature of the specific microRNAs responsible for this function. These miRNAs could then be used as markers for both the developmental potential of embryonic stem cells derived by various means as well as a marker for the appropriate silencing of self-renewal in ES cell derived tissues prior to transplant in patients. Furthermore, they could provide targets for therapeutic intervention in the unfortunate scenario of tumor formation from transplanted tissues that had failed to fully silence the stem cell program.

Statement of Benefit to California:

This grant proposes to identify the molecules that normally silence the potential of human embryonic stem cells to proliferate indefinitely. Identification of such molecules should benefit California in at least two ways. First, understanding the mechanisms our cells have evolved to silence indefinite proliferation would provide novel targets for therapeutic interventions in cancers either resulting spontaneously or from transplanted embryonic stem cell derivatives. Second, expression of these molecules should provide markers and, therefore, tests for analyzing the developmental and tumorigenic potential of embryonic stem cell derivatives pre- and post-transplant of these cells into patients. Such advances would benefit the health as well as the economy of the state of California.
